IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

ABBOTT GMBH & CO., KG, ABBOTT BIORESEARCH CENTER, INC., AND ABBOTT BIOTECHNOLOGY LTD.,	)	
Plaintiffs,	)	
v.	)	C.A. No. 4:09-CV-11340 (FDS)
CENTOCOR ORTHO BIOTECH, INC. AND CENTOCOR BIOLOGICS, LLC.,	)	JURY TRIAL DEMANDED
Defendant.	)	

DEFENDANTS' SUPPLEMENTAL
CLAIM CONSTRUCTION BRIEF

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Pursuant to the Court's invitation at the November 9 claim construction hearing, Defendants Centocor Ortho Biotech, Inc. and Centocor Biologics, LLC (collectively "Centocor") hereby submit this supplemental brief in support of their proposed constructions of disputed terms appearing in the asserted claims of U.S. Patent 6,914,128 (the "128 patent") and 7,504,485 (the "485 patent") (collectively, "the asserted patents").

I. 128 Patent – "neutralizing antibody"

A. The Parties Now Appear to Be in Agreement

Based on Abbott's arguments at the November 9 hearing, it appears that Abbott agrees that the activity being neutralized by the claimed antibodies is an activity caused **by the antigen to which the antibody is bound**, not an activity caused by any other cytokine or even any other event or agent. That being the case, there should be no dispute about the construction of "neutralizing antibody" in the 128 patent claims or of "neutralizing" in the 485 patent claims (the latter not having been a term for which construction had been sought).

Claims 7 and 29 in the 128 patent use the term "neutralizing antibody," as follows:

> 7. The isolated antibody of any one of claims 1 to 3, wherein the antibody is a **neutralizing antibody**. [Claims 1 to 3 each recite an antibody "that binds to human IL-12".]
>
> 29. An **neutralizing** isolated human **antibody**, or antigen-binding portion thereof that binds to human IL-12 and disassociates from human IL-12 with a K_{off} rate constant of $1x10^{-2}$ s^{-1} or less, as determined by surface plasmon resonance.

Centocor contends that the construction of "neutralizing antibody" should require that the antibody's binding to human IL-12 result in inhibition of a biological activity **of IL-12**. In its briefing, Abbott contended that "neutralizing" antibody only requires that the antibody inhibit a biological activity, leaving open the possibility that the antibody could neutralize activity caused by other cytokines or agents.

But from Abbott's counsel's comments at the *Markman* hearing, it appears that Abbott agrees that "neutralizing antibody" in the context of the 128 patent claims, which recite antibodies that bind to IL-12, means that the antibodies neutralize (*i.e.*, inhibit biological activity) of **IL-12 activity**:

> MR. LEE: What I said, your Honor, is that if you look at the context of the claim – I think this is what we said in the reply. The claims refer to IL-12. **So when you're referring to the neutralization, you're referring to IL-12.** That's the point we made about there's context to the claim beyond just the word neutralizing.

(Pearson 2nd Decl., Ex. 4, Tr. at 78:17-23). Thus, Abbott appears to agree with Centocor's proposed construction of "neutralizing antibody" in the 128 patent.

Following the same reasoning, a consistent construction of "neutralizing" as used in the 485 patent claims may be adopted.[1] The parties had not sought construction of "neutralizing" in the context of the 485 patent claims. At the hearing, Abbott's counsel pointed to the use of the term "neutralizing" in the 485 patent claims. Claims 15 and 25 of the 485 patent recite:

> 15. A pharmaceutical composition comprising an isolated human antibody, or antigen-binding portion thereof, which is capable of binding to an interleukin comprising a p40 subunit, and further comprising an additional agent.
>
> 25. The composition of claim 15, wherein the antibody, or antigen binding portion thereof, **neutralizes** a biological activity of the interleukin.

As Centocor understands Abbott's argument, Abbott contended that "neutralizing antibody" in the 128 patent could not be construed as limited to neutralization of IL-12 activity if it would mean that "neutralizes" in the 485 patent would also be limited to neutralization of IL-12 activity – because the 485 patent claims are not facially limited to antibodies that bind to IL-12. But the terms can be construed consistently between the patents if the recited neutralization

[1] Although "neutralizing antibody," used in the 128 patent claims, is expressly defined in the patents (e.g., Pearson Decl. Ex. 2, 128 Patent at 27:53-65), "neutralizing" is not.

activity in each patent is neutralization of the antigen **to which the antibody is bound**. In other words, the 128 patent claims recite only antibodies that bind to IL-12, so the recited neutralization activity is neutralization of IL-12, the antigen to which the antibodies are bound. The 485 patent claims recite only antibodies capable of binding to an interleukin having a p40 subunit, and the neutralization recited in Claim 25 should be neutralization of the biological activity of the interleukin **to which the antibody is bound**.[2]

B. Abbott Appears to Have Withdrawn its Accusation that Centocor Counsel was Arguing Inconsistently

Centocor relied on the *Noelle*[3] decision in its briefs and at the November 9 hearing as relevant to consideration of what antibodies are fairly described in the asserted patents. Abbott's counsel suggested at the hearing that Centocor's counsel had, at an appellate argument a week earlier, made arguments contrary to the arguments presented at the claim construction hearing (Pearson 2nd Decl. Ex. 4, Tr. at 58:10-21, 75:22-76:12). Abbott's counsel represented that he would advise Centocor's counsel of the portion of the appellate argument transcript on which he was relying for this accusation (*id*. at 125:6-12). Abbott subsequently advised Centocor that it had decided "it is unnecessary, so we will not be relying on the argument from the Federal Circuit in our Nov. 19 submission" (Pearson 2nd Decl. Ex. 5, 11/15/2010 Watson email to Pearson).

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[2] Centocor does not agree that the 485 patent claims, which encompass antibodies to interleukins not described in the patent, are valid, but validity is an issue for another day.

[3] *Noelle v. Lederman*, 355 F.3d 1343 (Fed. Cir. 2004).

II. The Assay Claims

A. Centocor's Constructions are Consistent with Abbott's Agreement that "Neutralizing Antibody" in the 128 Patent Refers to an Antibody that Neutralizes IL-12 Activity

Abbott's apparent agreement at the hearing that a "neutralizing antibody" recited in certain 128 patent claims is, as Centocor has asserted, an antibody that inhibits **IL-12** activity provides further support for aspects of Centocor's constructions of assay claim terms.

Centocor contends that "inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA blast assay" means "inhibits the proliferation of human PHA blasts **stimulated by IL-12**." Centocor also contends that "inhibits IFNγ production" means "inhibits the production of human interferon-γ by human PHA blasts **stimulated by IL-12**." In other words, just as a "neutralizing antibody" in the 128 patent claims is an antibody that inhibits **IL-12** activity, these assay claim terms refer to biological activities of **IL-12** being neutralized or inhibited.

Abbott argued for the first time at the November 9 hearing that Centocor's constructions of these assay terms were inconsistent with the use of the same terms in Claim 26 of the 485 patent. Validly or not, Claim 26 purports to cover compositions of antibodies that bind to interleukins **in addition to** IL-12. It recites the antibodies (by reference to claim 15) as being an antibody "which is capable of binding to an interleukin comprising a p40 subunit." That being the case, Centocor contends that the assay terms in Claim 26 of the 485 patent should be construed consistently with what Centocor proposes above for construction of "neutralizing" in the 485 patent claims. Specifically, **in the context of the 485 patent**,

> "inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay" means "inhibits the proliferation of human PHA blasts stimulated **by the interleukin to which the antibody is bound**"
>
> and

> "inhibits human IFNγ production" means "inhibits the production of human interferon-γ by human PHA blasts **stimulated by the interleukin to which the antibody is bound**."

B. Centocor's Constructions do not Improperly Import Limitations into the Claims

At the November 9 hearing, the Court made note of the difficulty of following the Federal Circuit's directive to construe claims in light of the specification while avoiding improperly importing limitations from the specification into the claims. The Federal Circuit has also commented on the tension between these directives. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1323 (Fed. Cir. 2005) (*en banc*). The court has advised that, to avoid improperly importing limitations into the claims, one must keep in mind that "the purposes of the specification are to teach and enable those of skill in the art to make and use the invention and to provide a best mode for doing so." *Id.* (citing *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1533 (Fed. Cir. 1987)). The court further stated:

> One of the best ways to teach a person of ordinary skill in the art how to make and use the invention is to provide an example of how to practice the invention in a particular case. Much of the time, upon reading the specification in that context, it will become clear whether the patentee is setting out specific examples of the invention to accomplish these goals, or whether the patentee instead intends for the claims and the embodiments in the specification to be strictly coextensive.

Phillips, 415 F.3d at 1323.

Viewed in light of this "guidance," the correctness of Centocor's construction of the "assay" claim terms is apparent. Nothing in the patent suggests that the assay limitations recited in the claims could be divorced from the descriptions of the assays in the patent, namely, the descriptions in Example 3. Those descriptions, even though they are provided in an "example," are the **only** teaching in the patent of how to determine whether an antibody has the required IC_{50}

values, and nothing in the patent suggests that other, undisclosed assays could be invented or used to measure the antibody properties.[4]

III. 485 Patent – "additional agent"

Centocor contends that "additional agent" as used in the 485 patent claims must be construed to **exclude** agents which are pharmaceutically acceptable carriers because Abbott disclaimed coverage for pharmaceutically acceptable carriers during prosecution of the 485 patent.

A. Abbott's Claim Amendment Was a Clear and Unambiguous Disavowal

At the November 9 hearing, Abbott's counsel seemingly suggested that there can be no disavowal of claim scope absent an express statement from Abbott that it was giving up pharmaceutical carriers (see, *e.g.*, Pearson 2nd Decl. Ex. 4, Tr. at 116:8-24). But an express statement of what is being surrendered is not necessary for there to be a clear and unambiguous disavowal. In fact, commentary in several Federal Circuit cases suggests that an amendment surrendering coverage – as was the case in the 485 patent prosecution history – is itself a clear and unambiguous disavowal. *See, e.g., Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1327 (Fed. Cir. 2003) ("the prosecution history may not be used to infer the intentional narrowing of a claim absent the applicant's clear disavowal of claim coverage, **such as an amendment to overcome a rejection**") (emphasis added); *York Prods., Inc. v. Central Tractor & Family Ctr.*, 99 F.3d 1568, 1575 (Fed. Cir. 1996) ("**unless altering claim language to escape an examiner rejection**, a patent applicant only limits claims during prosecution by clearly disavowing claim coverage") (emphasis added).

[4] As noted at the hearing, the statement at Column 27, lines 62-65 of the 128 patent cannot be fairly read to mean that other assays "known in the art" could be used to measure the specific IC_{50} values recited in the claims. For one thing, the reference to "Example 3" in that sentence points the reader to the descriptions in Example 3. For another, to the extent the sentence is construed to refer to assays other than those in Example 3, the reasonable reading is that these additional "known in the prior art" assays measure biological activities other than the PHA, IFNγ, and RBA activities recited in the claims.

A case on point is *Lemelson v. General Mills, Inc*., 968 F.2d 1202 (Fed. Cir. 1992). In response to a prior art rejection and pursuant to the patent examiner's suggestion during prosecution of his patent application, Lemelson had narrowed his claims by adding limitations to them. In the course of later litigation, Lemelson tried to advance a construction of his claims that ignored the added limitations. But the Federal Circuit said,

> Lemelson cannot acquiesce to a rejection and to an agreed alternative, and now years later shift his stance 180º to argue for a second bite at the abandoned apple. Other players in the marketplace are entitled to rely on the record made in the Patent Office in determining the meaning and scope of the patent.

Id. at 1207-08.

Lemelson is analogous to the instant case. Abbott amended its claims – adding the "additional agent" language – "to incorporate the limitations of the dependent claims which the Examiner has indicated do not interfere with the claims of the '994 application" (Ex. 8 to Centocor opening brief, at COBI01290441). The patent examiner expressly noted that the amendments Abbott made were "to incorporate limitations of the dependent claims which do not interfere with the claims of the '994 application" (Pearson 2nd Decl. Ex. 6 at ABT-IL12-03614763). The examiner also expressly stated that the amended claims "do not interfere with the claims of US Application No. 10/912,994, ***and are therefore allowable***" (*id*., emphasis added). There was a clear meeting of the minds between Abbott and the patent examiner as to just what was being given up, and as to the benefit accruing to Abbott because of the relinquishment of claim scope. This is a clear and unambiguous disclaimer, and, paraphrasing *Lemelson*, Centocor is "entitled to rely on the record made in the Patent Office in determining the meaning and scope of the patent."

B. The Comparison to 128 Patent Claim 64 is Appropriate

Abbott erroneously suggests that its disclaimer is not clear and unambiguous because the proper comparison is between the amended claims in the 485 patent and the Centocor 994 application claims, not between the amended claims in the 485 patent and Claim 64 of the 128 patent. But this is a distinction without meaning because the Centocor 994 application claims and the 128 patent claims, including Claim 64, were **directed to the same patentable invention**.

A patent interference proceeding determines whether two parties claim the same patentable invention and, if so, who is entitled to priority of invention. *Rolls-Royce, PLC v. Untied Techs. Corp.*, 603 F.3d 1325, 1330 (Fed. Cir. 2010). Here, the Patent Office declared that the claims of Centocor's 994 application and Claims 1-74 of Abbott's 128 patent were directed to the same invention, as defined by the "count" of the interference. (Pearson 2nd Decl. Ex. 7 at ABT-IL12-00298724); Pearson 2nd Decl. Ex. 8, 37 C.F.R. §41.201 ("count" defined as "description of the interfering subject matter")). Notably, in declaring that Abbott's Claims 1-15, 27-40 and 50-64 were all directed to the **same invention** as Centocor's 994 application antibody claims, the Patent Office made no "patentable distinction" between Abbott's antibody claims (Claims 1-15, 27-40 and 50-63) and its pharmaceutical composition claim (Claim 64). In other words, whether claims to antibodies or to a pharmaceutical composition, all were directed to the same patentable invention.

Thus, when Abbott amended its 485 patent claims so that they were not interfering with Centocor's 994 application claims, it was also amending them so that they were not interfering with its own 128 patent claims. If the amended claims had interfered with the 128 patent claims, they would have been part of the same patentable invention as the count of the interference, and the patent examiner would not have been willing to pass the 485 patent to issue while the interference proceedings were still on-going. So by amending the 485 patent claims, Abbott

relinquished coverage for any invention that the examiner deemed was the "same patentable invention" as claimed in the 128 patent and the Centocor 994 application.[5]

Abbott argues that there can be no disclaimer if the prosecution events are subject to more than one reasonable interpretation, but these events are **not** subject to more than one reasonable interpretation. These claims – which the examiner determined to **not** be interfering:

> **128 patent Claim 64:**
>
> A pharmaceutical composition comprising [antibody][6] and a pharmaceutically acceptable carrier.
>
> **485 application Claim 142:**
>
> A pharmaceutical composition comprising [antibody] and further comprising an additional agent.

can only be non-interfering if "additional agent" in Claim 142 is something other than a pharmaceutically acceptable carrier which imparts a beneficial attribute to the therapeutic composition.

IV. Conclusion

Centocor respectfully requests that the following claim constructions be adopted:

128 patent – "neutralizing antibody"	An antibody whose binding to human IL-12 results in inhibition of a biological activity of human IL-12
485 patent – "neutralizes"	Results in inhibition of a biological activity of the interleukin to which the antibody is bound
128 patent – "inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay"	Inhibits the proliferation of human PHA blasts stimulated by IL-12
485 patent - "inhibits phytohemagglutinin	Inhibits the proliferation of human PHA

[5] As noted at the hearing, Centocor does not necessarily agree that the amended claims in the 485 patent are patentably distinct from the 128 patent claims, but the important point here is that the record reflects that Abbott and the examiner both understood the amendments to patentably distinguish the 485 patent claims from the subject matter of the interference.

[6] Note that, even though Claims 64 and 142 use different language to recite the antibodies, the examiner had determined that the antibodies as defined in the two claims were all part of the same invention, *i.e.*, were not patentably distinct. If that were not the case, he would not have required amendment of the 485 application claims so that they would not be interfering.

blast proliferation in an in vitro PHA assay"	blasts stimulated by the interleukin to which the antibody is bound
128 patent – "inhibits IFNγ production"	Inhibits the production of human interferon-γ by human PHA blasts stimulated by IL-12
485 patent – "inhibits IFNγ production"	Inhibits the production of human interferon-γ by human PHA blasts stimulated by the interleukin to which the antibody is bound
128 patent – "inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA)"	Inhibits IL-12 binding to IL-12 receptors on human PHA blasts
485 patent – "additional agent"	An agent, other than a pharmaceutically acceptable carrier, which imparts a beneficial attribute to the therapeutic composition

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that a true and correct copy of the foregoing Defendants' Supplemental Claim Construction Brief was electronically mailed to the following counsel of record on November 19, 2010 through the Court's ECF notification system.

Angela Verrecchio